Medication Adherence and Hospitalization Among Patients With Schizophrenia Treated With Antipsychotics

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Objective: **This analysis assessed rates of medication adherence and predictors of nonadherence and hospitalization among patients treated with long-acting injectable and oral antipsychotic therapies.** ***Methods:*** **Data were from a retrospective analysis of Florida Medicaid recipients with schizophrenic disorder (*ICD-9-CM* code 295.XX) who received a prescription for an antipsychotic between July 1, 2004, and June 30, 2005. Patients were required to have filled one additional antipsychotic prescription during follow-up. Adherence measures included medication possession ratio (MPR), medication persistence, medication consistency, and maximum gap in treatment. Multivariate logistic regression models identified predictors of nonadherence and hospitalization.** ***Results:*** **Patients were considered adherent if they had an MPR ≥.8. A total of 12,032 patients met selection criteria. The mean±SD MPR was .79±.23, medication persistence was 94.1%±16.4%, medication consistency was 83.3%±16.4%, and the maximum gap in treatment was 29.7±41.4 days. Thirty-seven percent of patients were hospitalized for any cause, and 32% had a psychiatric hospitalization. Predictors of nonadherence included newly starting treatment; younger age; a substance abuse diagnosis; use of a mood stabilizer, antidepressant, anxiolytic, or anticholinergic; and receipt of long-acting first-generation antipsychotics. Receipt of long-acting second-generation therapy or receipt of both first- and second-generation medications was associated with lower likelihood of nonadherence. Predictors of hospitalization risk included a diagnosis of other psychoses or substance abuse, anticholinergic use, and nonadherence to therapy.** ***Conclusions:*** **Results document rates of antipsychotic adherence and predictors of nonadherence and hospitalization. Findings may be useful to health plan administrators, formulary decision makers, and physicians. (*Psychiatric Services* 61:1239–1247, 2010)**

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Schizophrenic disorders afflict approximately 1.1% of the adult population, or 2.4 million people in the United States (1). Symptoms of schizophrenic disorders range from hallucinations and delusions to difficulty expressing emotion, communicating, developing plans, and finding pleasure in daily activities (2). Patients are usually treated with first- or second-generation antipsychotic medications.

Nonadherence to pharmaceutical therapy is common when patients are required to take medications on a long-term basis, and it has been found to be particularly prevalent in the case of schizophrenic disorders, which require continued use of a drug for daily functioning (2). Patients may be nonadherent to prescribed medications for many reasons, including forgetting to take the medication, feeling that the medication is unnecessary, or disliking the side effects (3,4). Previous studies have found that patients with schizophrenic disorders who are nonadherent to therapy are more likely to experience relapse of symptoms and repeated hospitalizations and that with each relapse the likelihood that the patient returns to his or her baseline level of functioning declines (5–13).

Long-acting antipsychotic medications are expected to improve treatment adherence through confirmed

medication delivery (injection versus oral) and increased monitoring (monthly office visits versus pharmacy refills for acquiring medication) (14,15). It has been shown that patients who switch to long-acting second-generation therapies tend to be at least as adherent as they were on oral therapies (16). Furthermore, studies indicate that patients who have previously been nonadherent with oral antipsychotics may be more adherent with long-acting second-generation therapy (17). A long-acting form of risperidone, a second-generation antipsychotic, has been approved for use in the United States (Risperdal Consta, Ortho-McNeil Janssen Pharmaceuticals). This long-acting formulation may have the advantage of providing the efficacy and safety benefits of second-generation antipsychotic therapy along with the adherence benefits of a long-acting delivery (12,18).

Limited data are available comparing medication adherence rates associated with well-established oral antipsychotic medications and the newer long-acting second-generation therapies. The goals of this retrospective database study were to assess rates of medication adherence by type of antipsychotic treatment received and to examine predictors of medication nonadherence and hospitalization.

Methods

Overview

This study involved a claims-based, retrospective cohort analysis of Florida Medicaid recipients who were not dually eligible for Medicare, who had at least one inpatient or two outpatient claims indicating a schizophrenic disorder, and who received an antipsychotic between July 1, 2004, and June 30, 2005 (index prescription). Study patients were required to be continuously eligible for Medicaid benefits from one year before through one year after the index prescription and to have filled one additional antipsychotic prescription during follow-up. Study measures included medication adherence (that is, medication possession ratio [MPR], medication persistence, medication consistency, and maximum continuous gap in treatment) and hospitalization (psychiatric and any cause). Multivariate logistic regression models were used to identify predictors of nonadherence and hospitalization.

Data source

This study was based on eligibility data, paid medical claims (inpatient and outpatient), and pharmacy claims from the Florida Medicaid program. Florida Medicaid is the nation's fourth largest state Medicaid program, covering more than 2.1 million people and having expenditures of $11 billion in 2005. Approximately 44% of expenditures went toward institutional services (inpatient stays and long-term care), 18% toward prescription drugs, 8% toward home health care, 6% toward physician visits, and 24% for other services.

Medicaid claims included patient characteristics (that is, age and gender) as well as a monthly history of eligibility for Medicaid and Medicare (that is, dual eligibility). Claims for prescription drugs included National Drug Code (NDC), dispense dates, quantities of medication dispensed, and number of days supplied. Inpatient medical service claims contained a primary diagnosis and up to four secondary diagnoses in *ICD-9-CM* format, a procedure code (if relevant) also in *ICD-9-CM* format, the admission date, and the number of inpatient days. Outpatient medical service claims included the primary diagnosis, up to four secondary diagnoses, a procedure code (if relevant), and the service date. The data used in this study covered the period from July 2003 through June 2006.

Patient selection and follow-up

Patients were selected if they met the following inclusion criteria: had one inpatient or two outpatient medical claims indicating a primary or secondary diagnosis of a schizophrenic disorder (*ICD-9-CM* code 295.XX) and filled at least one prescription for an antipsychotic medication between July 1, 2004, and June 30, 2005 (index prescription); were continuously eligible for Florida Medicaid benefits from one year before the index prescription (baseline period) through one year after the index prescription (follow-up period); were not dually eligible for Medicaid and Medicare benefits during the study period; and filled at least one prescription for an antipsychotic medication during follow-up.

Patients were assigned in a hierarchical fashion to one of five mutually exclusive study cohorts based on the types of antipsychotic medications prescribed to them at any point during the follow-up period. The long-acting second-generation therapy cohort included patients who filled at least one prescription for a long-acting second-generation antipsychotic without regard to other antipsychotics prescribed. The long-acting first-generation cohort included patients who filled any long-acting first-generation antipsychotic prescription and did not fill a long-acting second-generation antipsychotic prescription. The oral first- and second-generation cohort included patients who filled both oral first- and second-generation antipsychotic prescriptions and did not fill long-acting antipsychotic prescriptions. The oral second-generation only cohort included patients who filled oral second-generation antipsychotic prescriptions only, and the oral first-generation cohort included patients who filled oral first-generation antipsychotic prescriptions only. Because this was a retrospective database analysis using previously collected deidentified health care claims, no institutional review board approval was necessary.

Study measures

Medication adherence. Four alternative measures of medication adherence were assessed. The MPR was defined as the number of unduplicated, ambulatory (not hospitalized) days during which medication was available, divided by the number of days in the follow-up period. Persistence was defined as the number of days between the first and last antipsychotic prescription divided by the number of days remaining in the follow-up period after the first antipsychotic prescription was filled. Consistency was measured for each antipsychotic as the number of available medication days during follow-up for that antipsychotic divided by

the number of days from the first to the last antipsychotic prescription observed in the follow-up period. Overall consistency was calculated by weighting each of the drug-specific consistencies by the percentage of available medication time during follow-up for the respective medication. The maximum continuous gap in therapy was calculated as the maximum number of consecutive days during which the patient did not fill a prescription for or receive an injection of an antipsychotic treatment, starting from the end of the days supplied or 14 days after last injection for long-acting second-generation therapy and 28 days after last injection for long-acting first-generation therapy. Periods of hospitalization were excluded from these calculations because it was not possible to observe medications received in the hospital. Consistent with previous literature, patients were considered nonadherent to therapy if they had an MPR <.8 and were considered adherent to therapy if they had an MPR ≥.8 (11,17,19).

Hospitalization. Hospitalizations for psychiatric and for all causes were evaluated at the individual patient level as whether or not the patient had one or more hospitalizations and at the overall level as the percentage of patients with one or more hospitalizations. Psychiatric hospitalizations were defined as those with a primary or secondary *ICD-9-CM* diagnosis code in the range 290.XX to 319.XX (this was also explored on the basis of primary diagnosis only), whereas all-cause hospitalizations included all hospitalizations without regard to diagnosis.

Data analyses

Descriptive analyses were undertaken to evaluate differences across treatment cohorts in baseline and demographic characteristics. Baseline comorbidity was assessed in terms of presence of selected comorbidities defined using Deyo-Charlson definitions (20,21). Concomitant diagnoses of substance abuse (*ICD-9-CM* codes 303.XX to 305.XX and V654.2) and other psychotic conditions including dementia and bipolar disorder (*ICD-9-CM* codes 290.XX to 299.XX, excluding 295.XX) were assessed in the baseline period, as were selected concomitant medications (that is, antidepressants, anticholinergics, mood-stabilizing agents [for example, lithium], and anxiolytics).

Unadjusted analyses of medication adherence during follow-up are reported overall and by antipsychotic treatment cohort. To compare differences across study cohorts with regard to baseline demographic and clinical characteristics and adherence measures, an F test was used. Pairwise differences in demographic and clinical characteristics and adherence measures were compared using F tests between the oral first-generation only cohort (reflecting the most commonly used antipsychotics in general) and each of the other cohorts as well as between the long-acting second-generation cohort (reflecting the newest available antipsychotic) and each of the other cohorts. Unadjusted analyses of hospitalizations during follow-up are reported as the percentage of patients hospitalized overall and by level of adherence (that is, nonadherent versus adherent).

Multivariate logistic regressions were used to identify predictors of medication nonadherence and hospitalization (any cause and psychiatric). The model estimating the likelihood of medication nonadherence included the following potential predictors: patient age category (that is, younger than 34 years, 35 to 44 years, and 45 years and older), baseline concomitant psychiatric diagnoses (that is, substance abuse and other psychoses), use of selected concomitant medications (that is, antidepressants, anticholinergics, mood-stabilizing agents, and anxiolytics), newly starting antipsychotic treatment (that is, first antipsychotic medication received during the three months before the index prescription), and inclusion in the antipsychotic treatment cohort. The hospitalization models included as possible predictors patient age, concomitant psychiatric diagnoses, use of selected concomitant medications, newly starting antipsychotic treatment, and level of adherence. Alternative specifications including interactions between antipsychotic type and demographic and clinical parameters were tested; however, no interaction terms were statistically significant. All analyses were conducted using SAS, version 9.1.

Results

We identified 15,979 patients who had at least one inpatient or two outpatient diagnoses of schizophrenia, had at least one claim for an antipsychotic prescription in the patient selection window, and were not dually eligible for Medicare and Medicaid benefits. Of those, 12,032 (75%) had at least one additional antipsychotic claim during follow-up and were eligible for benefits from one year before to one year after the index prescription. Most patients were in the oral second-generation only cohort (65%), followed by the oral first- and second-generation cohort (14%), the long-acting first-generation cohort (11%), the long-acting second-generation cohort (5%), and the oral first-generation only cohort (5%) (Table 1). The mean age of the patients was 43.2±13.0 years.

In the baseline period, 31% of patients had a diagnosis of chronic obstructive pulmonary disease (range of 21% in the oral first-generation only cohort to 34% in the oral first- and second-generation cohort) and 19% had a diagnosis of diabetes (range of 14% in the long-acting second-generation cohort to 19% in the oral first- and second-generation cohort). Eighteen percent of patients had a medical claim indicating a substance abuse diagnosis (range of 10% in the oral first-generation only cohort to 26% in the long-acting second-generation cohort), and 39% of patients had a claim indicating a diagnosis of other psychoses (range of 23% in the oral first-generation only cohort to 49% in the long-acting second-generation cohort), primarily bipolar disorder and other nonorganic psychoses.

Furthermore, 10% of all study patients were newly starting antipsychotic therapy, 61% received antidepressant medications, 50% received anxiolytic medications, and 43% received anticholinergic medications. Patients in the oral second-generation cohort had the highest use of antidepressants (67%) and anxiolytics

Table 1

Baseline demographic characteristics of Florida Medicaid recipients with a schizophrenic disorder who received a prescription for an antipsychotic, by cohort and overall[a]

Characteristic	Oral first-generation only (cohort 1) (N=640)		Oral second-generation only (cohort 2) (N=7,790)		Oral first- and second-generation (cohort 3) (N=1,688)		Long-acting second-generation (cohort 4) (N=643)		Long-acting first-generation (cohort 5) (N=1,271)		Total (N=12,032)		Comparison[b]	
	N	%	N	%	N	%	N	%	N	%	N	%	A	B
Age													2,3,4,5	2,3,5
<18	3	<1	399	5	39	2	23	4	10	1	474	4		
18–34	63	10	1,572	20	362	21	199	31	217	17	2,413	20		
35–44	150	23	1,818	23	440	26	189	29	375	30	2,972	25		
45–64	403	63	3,841	49	826	49	224	35	654	51	5,948	49		
≥65	21	3	160	2	21	1	8	1	15	1	225	2		
M±SD	48.1±10.3		42.9±13.6		43.0±12.2		39.5±12.7		44.4±11.2		43.2±13.0			
Median	49		45		45		41		45		45			
Interquartile range	42–56		34–53		35–52		29–48		38–52		35–52			
Male	327	51	3,539	45	846	50	332	52	675	53	5,719	48	2	2
Race														
White	242	38	2,972	38	660	39	249	39	386	30	4,509	37	5	5
Black	209	33	1,610	21	489	29	212	33	516	41	3,036	25		
Other	184	29	3,125	40	524	31	171	27	364	29	4,368	36		
Unknown or missing	5	1	83	1	15	1	11	2	5	<1	119	1		
Concomitant medication														
Antidepressant	269	42	5,186	67	1,010	60	353	55	563	44	7,381	61	2,3,4	2,5
Anxiolytic	264	41	4,109	53	887	53	247	38	536	42	6,043	50	2,3	2,3
Mood stabilizer	38	6	412	5	111	7	58	9	74	6	693	6		2,5
Anticholinergic	407	64	2,544	33	985	58	373	58	895	70	5,204	43	2,5	2,5
New start[c]													2,4	5
Yes	37	6	858	11	162	10	76	12	90	7	1,223	10		
No	603	94	6,932	89	1,526	90	567	88	1,181	93	10,809	90		
Concomitant diagnosis														
Substance abuse	65	10	1,263	16	396	23	166	26	272	21	2,162	18	2,3,4,5	2
Other psychoses[d]	150	23	3,027	39	733	43	318	49	460	36	4,688	39	2,3,4,5	2,5
Selected comorbidity														
Chronic obstructive pulmonary disease	134	21	2,427	31	576	34	178	28	383	30	3,698	31	2,3,5	3
Diabetes without chronic complications	110	17	1,499	19	329	19	88	14	238	19	2,264	19		2,3

[a] Source: Florida Medicaid 2003–2006 (excludes patients dually eligible for Medicare and Medicaid). Statistically significant differences across study cohorts were found for all variables using F test ($p<.01$).

[b] Comparison A is the comparison between cohort 1 and each of the other cohorts. Comparison B is the comparison between cohort 4 and cohorts 2, 3, and 5. Numbers in these columns reflect cohort numbers for which statistically significant differences were found ($p<.05$).

[c] New starts is defined as all patients who received their first antipsychotic three months before the index prescription.

[d] Other psychoses included *ICD-9-CM* diagnosis codes 290.XX to 299.XX, excluding 295.XX.

(53%), followed by patients in the oral first- and second-generation cohort (60% and 53%, respectively). Patients in the first-generation cohorts (long-acting and oral) had the highest rates of anticholinergic use (70% for the long-acting cohort and 64% for the oral cohort).

Differences in all demographic and clinical characteristics were statistically significant ($p<.01$) across study cohorts. Differences were statistically significant ($p<.05$) between the oral first-generation only cohort and the oral second-generation cohort in age; gender; use of antidepressants, anxiolytics, and anticholinergic agents; new starts; substance abuse; other psychoses; and chronic obstructive pulmonary disorder. Additionally, statistically significant differences ($p<.05$) were detected between the long-acting second-generation cohort and the oral second-generation only cohort in age; gender; use of antidepressants, anxiolytics, mood stabilizers, and anticholinergic agents; substance abuse; other psychoses; and diabetes. There were also statistically significant differences ($p<.05$) between the long-acting second-generation cohort and the long-acting first-generation cohort in age; race; new starts; use of antidepressants, mood stabilizers, and anticholinergic agents; and other psychoses.

Unadjusted analyses found that the mean MPR was .79±.23, average persistence was 94.1%±16.4%, and aver-

Table 2

Treatment adherence in the follow-up period among Florida Medicaid recipients with a schizophrenic disorder who received a prescription for an antipsychotic, by cohort and overall[a]

Characteristic	Oral first-generation only (cohort 1) (N=640)		Oral second-generation only (cohort 2) (N=7,790)		Oral first- and second-generation (cohort 3) (N=1,688)		Long-acting second-generation (cohort 4) (N=643)		Long-acting first-generation (cohort 5) (N=1,271)		Total (N=12,032)		Comparison[b]	
	N	%	N	%	N	%	N	%	N	%	N	%	A	B
Medication possession ratio													5	2,5
.8–1	448	70	5,015	64	1,195	71	460	72	788	62	7,906	66		
.5–<.8	116	18	1,608	21	296	17	134	21	241	19	2,395	20		
<.5	76	12	1,167	15	197	12	49	8	242	19	1,731	14		
Mean±SD	.81±.22		.79±.23		.82±.22		.84±.20		.77±.26		.79±.23			
Median	.91		.88		.92		.92		.9		.89			
Interquartile range	.74–.96		.68–.96		.75–.98		.77–.98		.63–.98		.70–.97			
Consistency (%)													5	5
M±SD	84.8±17.7		3.7±16.3		85.1±13.7		83.4±12.4		77.1±20.0		83.3±16.4			
Median	92.3		89.3		89.0		86.1		82.5		88.7			
Interquartile range	78.7–96.7		77.1–95.7		78.6–95.4		77.1–92.4		67.5–92.7		76.4–95.4			
Persistence (%)														
M±SD	95.0±15.5		93.5±17.3		95.2±14.8		95.9±14.4		95.0±13.9		94.1±16.4			5
Median	100.0		100.0		100.0		100.0		100.0		100.0			
Interquartile range	100.0–100.0		99.5–100.0		100.0–100.0		100.0–100.0		99.2–100.0		99.7–100.0			
Maximum gap in treatment (days)														
Mean±SD	25.3±34.5		30.2±41.4		25.7±37.9		25.1±35.3		36.8±50.0		29.7±41.4		2,5	2,5
Median	12.0		15.0		11.0		13.0		16.0		14.0			
Interquartile range	5.0–32.0		5.0–36.0		3.0–32.0		3.0–34.0		4.0–51.0		5.0–36.0			

[a] Source: Florida Medicaid 2003–2006 (excludes patients dually eligible for Medicare and Medicaid). There were statistically significant differences across study cohorts using for all variables the F test ($p<.001$).

[b] Comparison A is the comparison between cohort 1 and each of the other cohorts. Comparison B is the comparison between cohort 4 and cohorts 2, 3, and 5. Numbers in these columns reflect cohort numbers for which statistically significant differences were found ($p<.05$).

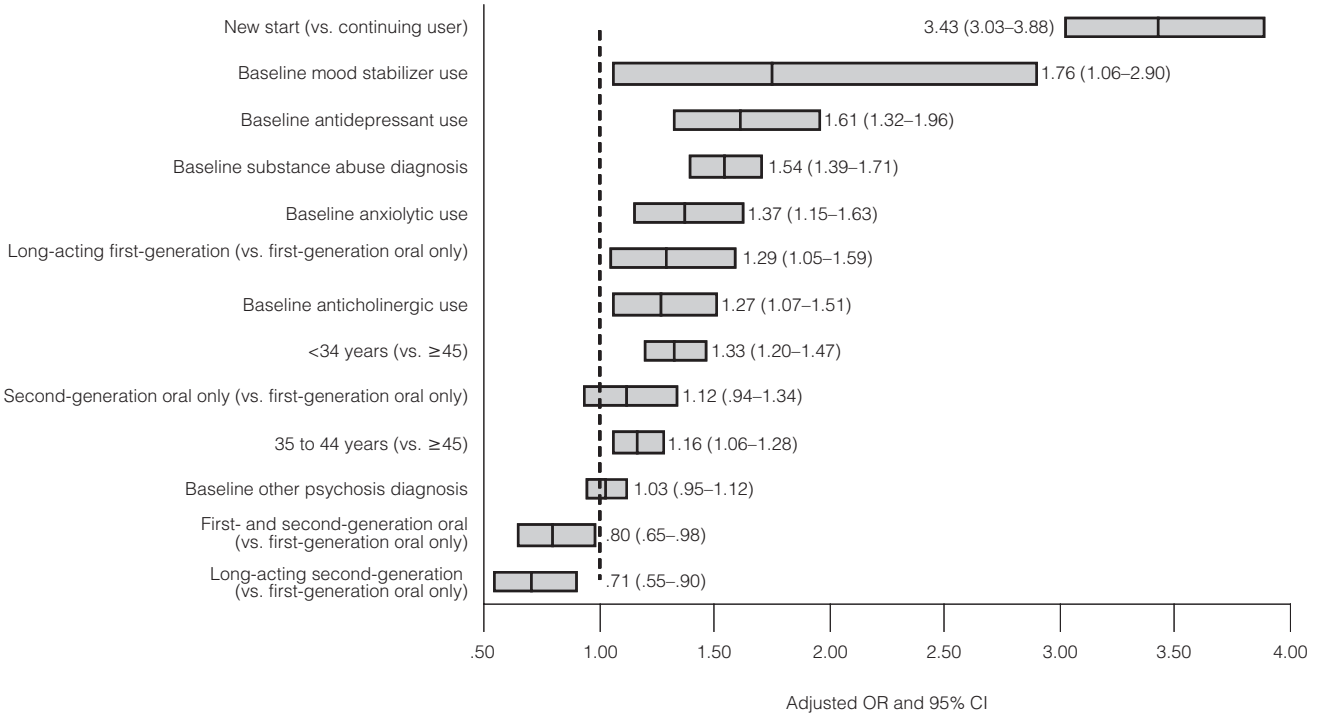
age consistency was 83.3%±16.4% across all study cohorts (Table 2). The mean maximum consecutive gap in treatment was 29.7±41.4 days. Some variation was noted in adherence measures across study cohorts. The mean MPR ranged from .77 for the long-acting first-generation cohort to .84 for the long-acting second-generation cohort. Mean persistence ranged from 93.5% for the oral second-generation only cohort to 95.9% for the long-acting second-generation cohort. Mean consistency ranged from 77.1% for the long-acting first-generation cohort to 85.1% for the oral first- and second-generation cohort. The average maximum gap in treatment ranged from 25.1 days for the long-acting second-generation cohort to 36.8 days for the long-acting first-generation cohort. Differences in all adherence measures were statistically significant ($p<.001$) across study cohorts, and differences in MPR, consistency, and maximum gaps in treatment were statistically significant between the oral first-generation only cohort and the long-acting first-generation cohort ($p<.05$). Additionally, statistically significant ($p<.05$) differences in adherence measures were detected between the long-acting second-generation cohort and the oral second-generation only cohort (MPR, persistence, maximum gaps in treatment) and between the long-acting second-generation cohort and the long-acting first-generation cohort (MPR, consistency, maximum gaps in treatment).

Based on multivariate logistic regression, the strongest statistically significant predictors of an increased risk of nonadherence (MPR <.8) were newly starting antipsychotic treatment (odds ratio [OR]=3.43), followed by a baseline substance abuse diagnosis (OR=1.54) and baseline concomitant use of mood-stabilizing, antidepressant, anxiolytic, or anticholinergic medications (ORs=1.76, 1.61, 1.37, and 1.27, respectively) (Figure 1). Additionally, factors associated with a significantly greater risk of nonadherence included younger patient age (ORs=1.33 and 1.16 for patients younger than 34 years and 35 to 44 years, respectively, versus patients aged 45 years and older) and being in the long-acting first-generation cohort (versus oral first-generation only cohort) (OR=1.29). In contrast, patients who received long-acting second-generation therapy or both first- and second-generation medications (versus oral first-generation medications only) had a lower likelihood of nonadherence (ORs=.71 and .80, respectively).

A total of 4,424 patients (37%) were hospitalized for any reason during follow-up, while 3,801 of those patients (32%) were hospitalized with a mental disorder listed as the primary or secondary diagnosis (N=

Figure 1

Adjusted odds of medication nonadherence associated with characteristics of patients with schizophrenic disorders treated with antipsychotic medications[a]



[a] Nonadherence defined as a medication possession ratio <.8

2,900, 24%, based on primary diagnosis only). Compared with patients who were classified as adherent, those who were nonadherent were 26% more likely to be hospitalized for any reason (N=2,719, 34%, and N=1,763, 43%, respectively) and 27% more likely to be hospitalized with a psychiatric diagnosis (N=2,326, 29%, and N=1,521, 37%, respectively).

Multivariate logistic regression indicated that the strongest predictors of an increased risk of a psychiatric hospitalization included presence of a baseline diagnosis of substance abuse or other psychoses (OR=3.04 and 2.89, respectively), followed by baseline mood stabilizer use (OR=1.54), newly starting antipsychotic therapy (OR=1.40), baseline anticholinergic use (OR=1.35), having an MPR <.8 (OR=1.28), and being younger than 34 years (versus 45 years or older) (OR=1.14) (Figure 2). Patients were more likely to have a hospitalization for any reason if they had a diagnosis of substance abuse or other psychoses at baseline (OR=2.70 and 2.53, respectively), if they were newly prescribed antipsychotics (OR=1.42), if they had an MPR <.8 (OR=1.35), and if they had baseline anticholinergic or antidepressant use (OR=1.35 and 1.24, respectively) (Figure 3). Results were similar when psychiatric hospitalization was defined based on primary diagnosis only.

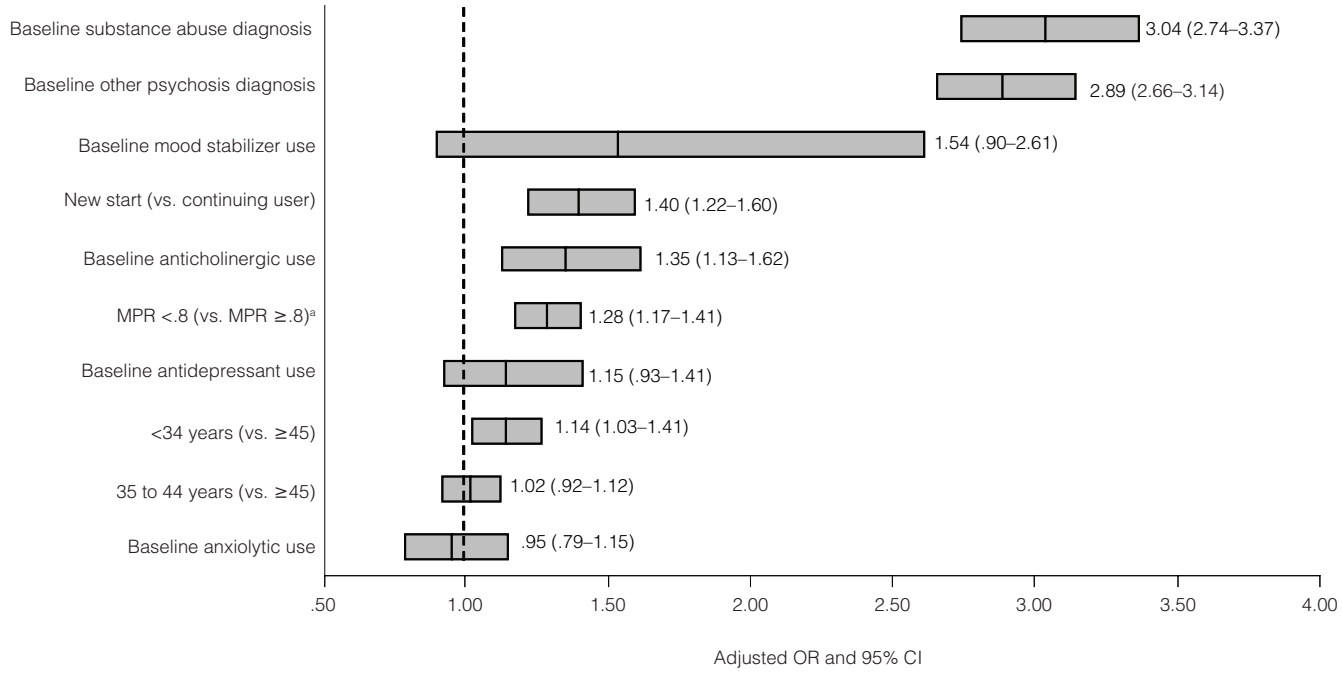
Discussion

This retrospective analysis of Florida Medicaid data examined rates of medication adherence and predictors of nonadherence and hospitalization among patients with schizophrenic disorders treated with long-acting therapies and daily oral therapies. To our knowledge, this is the first large-scale database analysis to evaluate predictors of medication nonadherence and hospitalization among patients with schizophrenic disorders since the introduction of long-acting second-generation therapies. We found that most patients were fairly adherent to antipsychotic treatment, as measured by the average overall MPR (.79), medication persistence (94.1%), and medication consistency (83.3%), and that there was relatively little variation in unadjusted adherence measures across treatment cohorts, with those who received long-acting second-generation therapy having the highest adherence rates. In multivariate analyses, older patients, those without concomitant psychiatric diagnoses or selected concomitant medications and those receiving either long-acting second-generation medications or first- and second-generation medications were found to have a significantly lower likelihood of nonadherence to therapy. Approximately one-third of patients were hospitalized during follow-up, with patients classified as nonadherent to antipsychotic therapy 26% more likely to be hospitalized than patients deemed to be adherent to therapy. Multivariate analyses found that significant predictors of an increased risk of all-cause or psychiatric hospitalization included concomitant psychiatric diagnoses and nonadherence to therapy.

There were noticeable differences in demographic and clinical characteristics across study cohorts. Patients who were receiving long-acting second-generation antipsychotics were

Figure 2

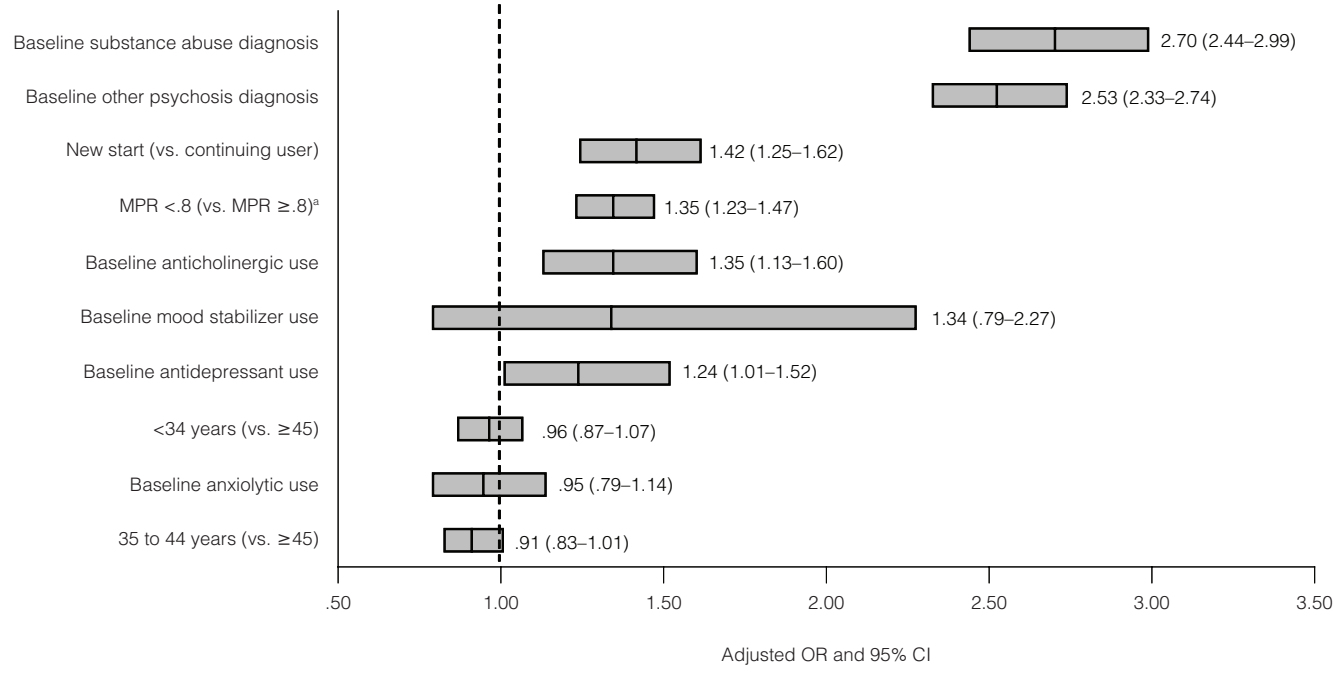
Adjusted odds of psychiatric hospitalization associated with characteristics of patients with schizophrenic disorders treated with antipsychotic medications



[a] Nonadherence defined as a medication possession ratio (MPR) <.8

Figure 3

Adjusted odds of all-cause hospitalization associated with characteristics of patients with schizophrenic disorders treated with antipsychotic medications



[a] Nonadherence defined as a medication possession ratio (MPR) <.8

the youngest, more likely to be black or white (versus other races), and more likely to have a new antipsychotic prescription. Patients in this cohort also seemed to be the most clinically complex, because they had the highest prevalence of diagnoses of substance abuse and other psychoses. Consistent with this, patients in the long-acting second-generation cohort had the highest unadjusted hospitalization rate (data not shown), suggesting that this type of medication is often administered to patients who require hospitalization.

Our overall findings regarding medication adherence rates are in line with other studies that have evaluated similar adherence measures among users of oral antipsychotic medications and long-acting first-generation formulations. In a study of California Medicaid recipients with schizophrenia treated with oral medications, Weiden and colleagues (13) found very similar results regarding mean MPR (.86 versus .79 in our study), persistence (97% versus 94% in our study), consistency (88% versus 83% in our study) and maximum gaps in treatment (28.4 days versus 29.7 days in our study). Two previous studies have compared oral second-generation and oral first-generation medications and have reported MPRs within the range of the analysis presented here (second-generation antipsychotics, MPRs of .79 and .94; first-generation antipsychotics, MPRs of .81 and .87) (9,11). We found higher estimates of MPRs compared with a study examining the MPR over the first 90 days of long-acting therapy (first-generation antipsychotics, .45 versus .77 in our study; second-generation antipsychotics, .40 versus .84 in our study) (17), and we found a lower MPR compared with a study looking at patients newly starting long-acting first-generation antipsychotics (.91 versus .77 in our study) (22). These differences may be attributable to the short time frame in the first study and to the fact that all patients were newly starting therapy in both studies.

Our unadjusted rate of psychiatric hospitalization was slightly higher than that reported previously (range of 7.4% to 27%) (7,9,10,13,23). Weiden and colleagues (13) and Svarstad and colleagues (7) both reported a larger unadjusted increased risk of hospitalization for nonadherent patients than that reported in our analysis (38% and 52%, respectively, versus 27% in our analysis). These differences may be due to alternative coding for psychiatric hospitalizations (13,23), the inclusion of dually eligible patients (7,10,13,23), or variations in adherence definitions (7,10).

Two previous studies (one of which used the same database as the current analysis) have presented OR estimates for predictors of nonadherence among patients treated with oral antipsychotics (10,24). Similar to our analysis, both of these studies found that patients who had a substance abuse diagnosis had a greater risk of nonadherence than those who did not. However, unlike our analysis, both reported that adherence decreased with increasing age. In contrast to our findings, Becker and colleagues (10) found that patients who received both first- and second-generation medications were more likely than patients who received first-generation medications only to be nonadherent to medication. Although our study noted no significant differences in adherence between oral second-generation and oral first-generation medications, previous studies of oral medications found that patients who received second-generation medications were more likely to be adherent than patients who received first-generation medications only (10,25). Differences in study populations or adherence methodologies may account for the difference in findings.

Finally, two previous studies have presented OR estimates for predictors of hospitalization among patients receiving oral antipsychotics (9,13). Similar to the analysis presented here, both studies found that patients who were nonadherent to therapy had a greater likelihood of hospitalization than patients who were adherent.

This study is subject to several limitations. Schizophrenic disorder diagnoses were not verified by medical chart reviews. Additional patient-level variables (for example, family involvement and living situation), which have been shown previously to affect adherence, could not be assessed (5,24). In addition, our findings may not apply to non-Medicaid populations or to patients dually eligible for Medicaid and Medicare. This study may overestimate adherence because treated days could not be confirmed among patients receiving oral therapies. Information was available only on the prescriptions filled, not medications actually taken. Adherence in the long-acting cohorts may not accurately reflect adherence to long-acting therapy because patients could have received other oral medications before receiving long-acting medications (few patients in the sample received only long-acting medications). Although our requirement that patients remain eligible for Medicaid benefits during the study period was necessary for tracking, it may have biased our sample to include patients who were more likely to remain adherent. Finally, this analysis was cross-sectional and did not attempt to evaluate the circular nature of the relationships among treatment type, adherence, hospitalization, and other variables; future work to disentangle this complex interaction is warranted.

Conclusions

After adjusting for baseline and demographic characteristics, we found that the risk of nonadherence to antipsychotic treatment was lowest among older patients, those without concomitant psychiatric diagnoses (substance abuse or other psychoses) or selected concomitant medications, and those receiving long-acting second-generation medications or oral first- and second-generation medications. Furthermore, our findings confirm that nonadherence is associated with a greater risk of hospitalization. These findings will be useful to health plan administrators, formulary decision makers, and physicians who treat patients with schizophrenic disorders.

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